Paper # **C 314**

Multi-Site Evaluation of Cefdinir, Linezolid, Meropenem, and Synercid on both the Sensititre Dried Susceptibility Panel and the NCCLS Microdilution Method

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ABSTRACT

A multi-site evaluation was undertaken comparing the performances of four new antimicrobials (cefdinir, linezolid, meropenem, and synercid) on the Sensititre 18 - 24 hour dried susceptibility panel to their performances with the NCCLS broth microdilution reference method. Both the autoread and manual methods were evaluated on the Sensititre system. The clinical evaluation was performed at two trial sites and consisted of 181 fresh clinical gram-positive isolates. These isolates included methicillin susceptible and resistant staphylococci, vancomycin susceptible and resistant enterococcus, and beta-hemolytic streptococci. The recommended quality control organisms were tested daily and were within the NCCLS expected quality control range.

The results for the four antimicrobials tested were as follows: For the autoread method verses the reference method the clinical isolates' essential agreements for cefdinir, linezolid, meropenem, and synercid were 100%, 96%, 98%, and 98%, respectively. For the manual read method verses the reference method the essential agreements were 100%, 99%, 98%, and 100%, respectively.

This multi-site evaluation indicated that the performances of cefdinir, linezolid, meropenem, and synercid on the Sensititre 18-24 hour dried susceptibility system were equivalent to their performances with the NCCLS broth microdilution reference method.

Since the initial submission of this abstract the total number of isolates that were tested has been increased from the original number of 181.

PURPOSE OF THE STUDY

To evaluate the performance of Cefdinir, Linezolid, Meropenem, and Synercid on the Sensititre 18 – 24 hour susceptibility panel compared to the NCCLS microdilution method (M7 - A4).

MATERIALS & METHODS

Organisms: The testing at 2 sites consisted of the following:
- 330 total clinical isolates (combined sites)
- 77 CDC challenge isolates per site
- 50 Enterococcus challenge isolates per site
- 10 reproducibility isolates (run in triplicate for 3 days)
- 2 Quality Control strains (run for 24 days per site)

Antimicrobials	Tested Range Tested	Supplied By:
Cefdinir (DIN)	0.060 – 32	Parke-Davis (Abbott)
Linezolid (LZD)	0.250 – 32	Pharmacia-Upjohn
Meropenem (MERO)	0.015 – 32	Zeneca
Synercid (SYN)	0.030 – 32	Rhone-Poulenc Rorer

Clinical Isolates Tested

Organism Species	Number Tested
Staphylococcus aureus	89
Staphylococcus epidermidis	56
Enterococcus faecalis	54
Enterococcus faecium	29
Staphylococcus species	30
Streptococcus species	43
Enterococcus species	29
Total	**330**

Susceptibility Testing Methods:
- Each isolate was tested using a Sensititre 18 – 24 susceptibility panel. The panels were set-up and tested according to the manufacturers' instructions.
- The reference panel was tested according to the microdilution methods published by the National Committee for Clinical Laboratory Standards (NCCLS, M7-A4).
- The approved primary "Indications for Use" and clinical significance of Cefdinir is for *Staphylococcus aureus* (MSSA) and *Streptococcus pyogenes*. In vitro data, without clinical correlation, is provided for: *Staphylococcus epidermidis* (MSSE) and *Streptococcus agalactiae*. Cefdinir is inactive against *Enterococcus* and methicillin-resistant *Staphylococcus species*.

RESULTS

Susceptibility Testing Methods:
- The approved primary "Indications for Use" and clinical significance of Linezolid is for *Enterococcus faecium* (VRE), *Staphylococcus aureus* (MSSA and MRSA), *Streptococcus agalactiae*, and *Streptococcus pyogenes*. In vitro data, without clinical correlation, is provided for *Enterococcus faecalis* (VSE and VRE), *Enterococcus faecium* (VSE), *Staphylococcus epidermidis* (MSSA and MRSA), and *Staphylococcus haemolyticus*.
- For Meropenem, In vitro data, without clinical correlation, is provided for *Staphylococcus aureus* (MSSA) and *Staphylococcus epidermidis* (MSSE). Meropenem is inactive against methicillin-resistant *Staphylococcus species*.
- The approved primary "Indications for Use" and clinical significance of Synercid is for *Staphylococcus aureus* (MSSA), *Streptococcus pyogenes, and Enterococcus faecium* (VRE and multi-drug resistant strains only). In vitro data, without clinical correlation, is provided for *Staphylococcus aureus (MRSA), Staphylococcus epidermidis* and *Streptococcus agalactiae*. Synercid is not active against *Enterococcus faecalis*.

Clinical Isolates Tested

Manual Read Method

Antimicrobials	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Cefdinir	175	85	94	66	4	0	7
Linezolid	330	98	98	0	0	0	1
Meropenem	218	89	98	23	0	0	5
Synercid	233	98	100	5	0	0	1

Autoread Method

Antimicrobials	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Cefdinir	175	83	91	66	8	0	8
Linezolid	330	94	100	0	0	0	1
Meropenem	218	86	96	22	1	0	7
Synercid	233	92	99	5	0	0	2

Enterococcus Challenge Isolates Tested

Manual Read Method

Antimicrobials	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Cefdinir	-	-	-	-	-	-	-
Linezolid	99	100	100	0	0	0	0
Meropenem	-	-	-	-	-	-	-
Synercid	59	98	100	8	0	0	0

Autoread Method

Cefdinir	-	-	-	-	-	-	-
Linezolid	99	95	100	0	0	0	0
Meropenem	-	-	-	-	-	-	-
Synercid	59	90	95	7	1	0	2

CDC Challenge Isolates Tested

Manual Read Method

Antimicrobials	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Cefdinir	77	94	99	23	0	0	1
Linezolid	154	100	100	0	0	0	0
Meropenem	87	94	97	4	0	1	2
Synercid	111	100	100	10	0	0	0

Autoread Method

Antimicrobials	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Cefdinir	77	86	95	23	2	0	2
Linezolid	154	96	99	0	0	1	0
Meropenem	87	89	98	4	0	0	2
Synercid	111	94	96	10	1	1	2

Reproducibility Isolates Tested
% Agreement Within ± 1 Dilution of Modal MIC

Antimicrobials	Autoread	Manual
DIN	97	99
LZD	96	100
MERO	96	95
SYN	97	98

CONCLUSION

This investigation compared the 18 – 24 hour Sensititre susceptibility panel with the standard microdilution panel (M7 - A4). The Sensititre panel demonstrated a high level of agreement and was very reproducible.

- **Clinical Isolates:**
  The overall essential agreement for the 4 drugs tested, within +/- one dilution, was 94% for the manual method and 90% for the autoread method.*
- **CDC Challenge Organisms:**
  The overall essential agreement for the 4 drugs tested, within +/- one dilution, was 98% for the manual method and 92% for the autoread method.*
- **Enterococcus Challenge Organisms:**
  The overall essential agreement for the 4 drugs tested, within +/- one dilution, was 99% for the manual method and 93% for the autoread method.
- **Reproducibility:**
  Interlaboratory reproducibility was 98% for the manual read method and 96% for the autoread method.

*The very major errors that are indicated in the "Results" section for Cefdinir occurred only when tested against coagulase-negative Staphylococcus species.